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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/491,982	01/27/2000	Stephen Shaughnessy	MDSP-P02-180	9313
28120	7590	05/25/2004	EXAMINER	
ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			MERTZ, PREMA MARIA	
			ART UNIT	PAPER NUMBER
			1646	

DATE MAILED: 05/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/491,982	<b>Applicant(s)</b> SHAUGHNESSY ET AL.	
	<b>Examiner</b> Prema M Mertz	<b>Art Unit</b> 1646	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE \_\_\_\_ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 4/22/04
- 2a) ☒ This action is **FINAL**.      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 3, 14, 43-50 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 3, 14, 43-50 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. ____.  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date ____.   | 6) <input type="checkbox"/> Other: ____.                                    |

### **DETAILED ACTION**

1. Claims 2, 4-13, 15-42 have been canceled previously. Claims 1, 3, 14, 43-50 are pending and under consideration by the Examiner.
2. Receipt of applicant's arguments and amendments filed on 4/22/2004 is acknowledged.
3. Applicant's arguments filed on 4/22/2004 have been fully considered but were non-persuasive. The issues remaining are stated below.
4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Claim Rejections - 35 USC § 103***

6. Claims 1, 3, 14, 43-49 are rejected under 35 U.S.C. 103 as being unpatentable over Girasole et al (1995) in view of Kishimoto et al. (US Patent No. 5,888,510).

This rejection is maintained for reasons of record set forth at pages 2-4 of the previous Office action (3/18/04).

Applicants argue that it was known at the time of the instant invention that IL-11 stimulated osteoclast function by eliciting IL-11 signaling in osteoclasts (see Girasole et al. 1994), osteoclasts being involved in bone resorption. It was also known at the time of the instant invention that osteoblasts contain IL-11 receptor (see Romas et al. 1995), osteoblasts being involved in bone formation. Applicants further argue that given the opposite functions of osteoclast and osteoblast in vivo, a skilled artisan would not know whether IL-11 administration to a patient in vivo would actually cause net bone formation or loss. However, contrary to Applicants' arguments, osteoblast involvement in bone formation and osteoclast involvement in bone resorption is a balancing process, which is constantly taking place in vivo.

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Therefore, a skilled artisan, from the teachings of the prior art would have an expectation of success knowing that a method of administering IL-11 antibody to a patient would increase osteoblast-mediated bone formation process and decrease osteoclast-mediated bone resorption process since these processes are in a constant balance.

Applicants appear to have misunderstood the application of the Kishimoto reference and are arguing the nexus between IL-6 and IL-11 as being too casual to provide a strong enough motivation to combine the references since there is no obvious structural similarity between IL-6 and IL-11 and the conditions to be treated by administering an IL-6 antibody (RA) and an IL-11 antibody (inhibiting reduction of bone density) are different. However, contrary to Applicants arguments, the Kishimoto reference has only been used for the proposition that if a cytokine is involved in a disease, an antibody to the cytokine will block the signal transduction by the cytokine, inhibit the cytokines biological activity and will have an alleviating and therapeutic effect on the symptoms of the disease (see column 3, lines 41-52). Furthermore, the Examiner has only to show a reasonable expectation of success. Therefore, at the time of the instant invention, based on the teachings of the prior art references, a person of skill in the art would have a reasonable expectation of success that administering IL-11 antibody would alleviate the effects of IL-11 signaling and would have a significant effect on bone density in vivo.

Furthermore, Applicants have only provided arguments on page 6 of the response and no substantial evidence for the premise that taking away one of the many cytokines in vivo that regulate the same function (such as bone formation or resorption) may or may not have a discernable effect on that biological function. In other words, Applicants have provided no

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evidence that the in vitro experiments would correlate in vivo. The Nandurkar et al. 1997 declaration is not on point because it demonstrates that there is no correlation between hematopoiesis in vitro and in vivo. This reference is not relevant because a completely different biological activity of IL-11 (effects on hematopoiesis) by "knocking out" the IL-11R is being argued by the Applicants and not a neutralizing effect on the IL\_11 cytokine by administering an antibody.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). If the Girasole et al. reference disclosed all the limitations of the instant claims this would be a 35 USC 102 rejection rather than a 35 USC 103 rejection. Therefore, from the combined teachings of Girasole and Kishimoto there is a definite nexus, which translates into a benefit for administering IL-1 1 antibodies for treating patients with decreased bone density.

7. Claim 50 is rejected under 35 U.S.C. 103 as being unpatentable over Girasole et al (1995) in view of Kishimoto et al. (US Patent No. 5,888,510) as applied to claims 1, 3, 14, 43-49 above, and further in view of Queen et al. (US Patent No. 5,530,101).

This rejection is maintained for reasons of record set forth at pages 4-5 of the previous Office action (3/18/04).

Applicants argue that the claimed invention is not obvious in view of Girasole and Kishimoto, and Queen does not in anyway correct these defects, even assuming a skilled artisan would be motivated to combine Queen with Girasole and Kishimoto to make humanized

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antibodies to inhibit osteoclast function. However, contrary to Applicants arguments, as asserted by the Examiner in paragraph 6 above, the combined teachings of Girasole and Kishimoto provide a reasonable expectation of success for one of ordinary skill in the art to combine the reference teachings. Therefore, the combined references, Queen with Girasole and Kishimoto render obvious the limitations of instant claim 50.

***Conclusion***

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (571) 271-0871.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications

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may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*Prema Mertz*  
Prema Mertz Ph.D.  
Primary Examiner  
Art Unit 1646  
April 28, 2004